

## REMARKS

Claims 11-22 are pending, original claims 1-10 having been cancelled in applicants' Preliminary Amendment of 22 June 2001.

Claims 19-21 have been cancelled herein.

Applicants acknowledge the Examiner's rejection of claims 11-17 and 19, under 35 U.S.C. § 112 ¶1, alleging new matter. Applicants respectfully traverse this rejection, based on applicants' original disclosure. Applicants have clarified the 'bisulfite-converted equivalents' language of claim 17 and 18 (now having the limitations of claim 19, cancelled herein).

Applicants acknowledge the Examiner's rejection of claims 17 and 19, under 35 U.S.C. § 112 ¶2, alleging indefiniteness in view of recitation of 'bisulfite-converted equivalents.' Applicants have clarified the 'bisulfite-converted equivalents' language of claims 17 and 18 (now having the limitations of claim 19, cancelled herein).

Applicants acknowledge the Examiner's rejection of claims 18 and 20-22, under 35 U.S.C. § 101, for statutory double patenting in view of applicants' U.S. Patent No. 6,251,594. Claim 18 has been amended to distinguish the claimed invention, and claims 20 and 21 have been cancelled. Applicants traverse the rejection with respect to claim 22, which depends from claim 11, which is subject to the Examiner's *provisional* non-statutory double patenting rejection.

Applicants acknowledge the Examiner's *provisional* rejections of claims 18 and 20-22, under the judicially-created doctrine of non-statutory double patenting in view of applicants' U.S. Patent No. 6,251,594, and in view of applicants' co-pending Application number 10/109,725. The present application is commonly owned with the allegedly conflicting Patent and Application, and applicants are prepared to file a Terminal Disclaimer in compliance with 37 C.F.R. 3.73(b) upon indication of allowable subject matter

No new matter has been added.

## FORMALITIES

Applicants thank the Examiner for indicating that the originally filed drawings are acceptable.

***Rejection under 35 U.S.C. § 112 ¶1; new matter***

The Examiner rejected claims 11-17 and 19, under 35 U.S.C. § 112 ¶1, as failing to comply with the written description requirement (Office Action of 28 November 2003, at page 2, paragraph 1).

***First***, essentially, the Examiner asserts that the specification as filed does not support recitation of ‘labeled dNTPs’ beyond  $^{32}\text{P}$ -dNTPs; that is, that the applicants did not have possession of the claimed invention at the time of filing.

***Second***, with respect to claims 17 and 19, the Examiner asserts that the specification as originally filed “does not provide basis for the concept of primers which are ‘the bisulfite-converted equivalents thereof.’”

Applicants respectfully traverse this rejection, based on the teachings of the originally filed Specification. Specifically, with respect to the ***first*** issue, the Specification at page 9, line 8, discloses and teaches the concept of using other labels “instead of a  $^{32}\text{P}$  marker” (e.g., fluorescent probes) in the context of the present invention. Significantly, applicants teach that the essence of the present invention is to determine methylation status by determining whether (e.g., for top strand analysis) the hybridized Ms-SNuPE primer is elongated (across the bisulfite-treated CpG sequence) with deoxy CTP or TTP; that is, to determine a C:T signal ratio (*see, e.g.*, Figure 2). Given this teaching, in combination with the recitation of “instead of a  $^{32}\text{P}$  marker,” one of ordinary skill in the art at the time of filing would understand from the instant teachings that the dNTPs could be labeled in any way that would allow for relative quantification of a C:T ratio.

Therefore applicants maintain that they were in possession, at the time of filing, of the broader claimed invention (“labeled dNTPs”), as recited in independent claim 11.

Applicants have amended ***dependent*** claim 12 to recite “radiolabels, fluorescent labels, and combinations thereof” to clarify the preferred embodiments as perceived by the inventors at the time of filing.

With respect to the ***second*** issue, applicants contend that the Examiner has inadvertently misconstrued the intended meaning of applicants’ claims language. The Specification does not

teach the use of bisulfite-treated primers, but rather teaches throughout that primers are used to hybridize to bisulfated-treated DNA. Thus, the intended meaning of ‘bisulfite-equivalents thereof’ in claims 17 and 19 is to include the bisulfite-treated sequences corresponding to SEQ ID NOS:1-12 in the recited Markush group. The meaning of bisulfite-treated DNA is disclosed throughout the original Specification, including on pages 7 and 8, and including the original claims.

Applicants have, nonetheless, amended the claim language in view of the Examiner’s comments to clarify the claimed invention. Specifically, claim 17 has been amended to recite “bisulfite-converted sequences corresponding to SEQ ID NOS:1-12.” Claim 19 has been cancelled herein, and its limitations have been introduced into independent claim 18, which, like 17 has been amended to recite “bisulfite-converted sequences corresponding to SEQ ID NOS:1-12.”

Support for this amendment is found throughout the Specification, for example: at the last paragraph of page 3 and first paragraph of page 4; page 4 lines 22-25; the transition paragraph between pages 7 and 8; etc. The specification teaches that bisulfite treatment converts unmethylated cytosine initially to Uracil, followed by conversion to Thymidine during amplification by primer extension in the present of dNTPs, (and this is in turn reflected in the choice of nucleotides (*e.g.*, C or T) chosen in the present invention to analyze Ms-SNuPE primer extension).

Preferably, as taught in the Specification at page 8, lines 30-33, the Ms-SNuPE primer is designed to hybridize to a region of bisulfite-treated DNA the sequence of which is not changed by the bisulfite-treatment. However, the invention is not limited to the preferred embodiments.

Applicants, therefore, respectfully request withdrawal of this 35 U.S.C. § 112 ¶1 rejection of claims 11-17 and 18 (now with the limitation of cancelled claim 19) in view of applicants’ arguments and claim amendments.

#### ***Rejection under 35 U.S.C. § 112 ¶2***

The Examiner rejected claims 17 and 19, under 35 U.S.C. § 112 ¶2, “as being indefinite...” (Office Action of 28 May 2003, at page 3).

Specifically, the Examiner asserts that the phrase “the bisulfite-converted equivalents” lacks antecedent basis, furthermore that it is unclear whether the phrase refers to bisulfite-treated primers or to primers that hybridize to bisulfite-treated DNA.

As described above in detail, applicants have amended claims 17 and 18 (now having the limitations of cancelled claim 19) to recite “bisulfite-converted sequences corresponding to SEQ ID NOS:1-12.”

Applicants, therefore, respectfully request withdrawal of the Examiner’s 35 U.S.C. § 112 ¶2 rejection in view of amended claims 17 and 18.

#### ***Double Patenting Rejection***

The Examiner has rejected claims 18 and 20-22, under 35 U.S.C. § 101 as claiming the same invention as that of claims 7 and 9-11 of prior U.S. Patent No. 6,251,594 (Office Action of 28 November 2003, at page 4, paragraph 3).

Applicants, as described above in detail, have amended claim 18 to incorporate the limitations of dependent claim 19 (cancelled herein), thus distinguishing the claimed invention from that of the ’594 patent.

Applicants have herein cancelled claims 20 and 21.

Applicants traverse this rejection with respect to claim 22, because it depends from claim 11 for which a provisional non-statutory rejection has been asserted as described below.

Applicants, therefore, respectfully request withdrawal of the Examiner’s statutory double patenting rejection.

#### ***Nonstatutory Double Patenting Rejection***

The Examiner has *provisionally* rejected claims 11-17 and 19, under the judicially created doctrine of non-statutory double patenting in view of U.S. Patent No. 6,251,594, and in view of applicants’ co-pending Application number 10/109,725 (Office Action of 28 November 2003, at page 4, paragraph 4).

Essentially, the Examiner asserts that some of the presently claimed subject matter, while

not identical to, is nonetheless overlapping with that of the '594 patent and the '725 application.

Applicants, as described above, have cancelled claim 19, incorporating its limitations into claim 18.

The present application is commonly owned with the allegedly conflicting Patent and Application, and applicants are thus prepared to file a timely Terminal Disclaimer in compliance with 37 C.F.R. 3.73(b) upon the Examiner's indication of allowable subject matter.

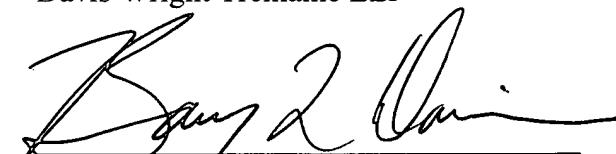
### CONCLUSION

In view of the foregoing amendments and remarks, applicants respectfully request entry of the present Response and Amendment, and allowance of all claims 11 (Previously added), 12-14 (all Currently amended), 15 and 16 (both Previously added), 17 and 18 (both Currently amended), and 22 (Previously added). No new matter has been added.

The Examiner is encouraged to phone applicants' attorney, Barry L. Davison, to resolve any outstanding issues and expedite allowance of this application.

Respectfully submitted,

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